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BIOCHEMISTRY

THIRD EDITION

LUBERT STRYER

STANFORD UNIVERSITY



EXHIBIT

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Part II PROTEIN CONFORMATION, DYNAMICS, AND FUNCTION

Torr-

A unit of pressure equal to that exerted by a column of mercury 1 mm high at 0°C and standard gravity (1 mm Hg).

Named after Evangelista
Torricelli (1608–1647), the inventor of the mercury barometer.

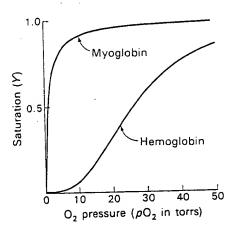


Figure 7-21
Oxygen dissociation curves of myoglobin and hemoglobin.
Saturation of the oxygen-binding sites is plotted as a function of the partial pressure of oxygen surrounding the solution.

HEMOGLOBIN IS AN ALLOSTER PROTEI

The α and β subunits of hemoglobin have the same structural design as myoglobin. However, new properties of profound biological importance emerge when different subunits come together to form a tetramer. Hemoglobin is a much more intricate and sentient molecule than is myoglobin. Hemoglobin transports H^+ and CO_2 in addition to O_2 . Furthermore, the oxygen-binding properties of hemoglobin are regulated by interactions between separate, nonadjacent sites. Hemoglobin is an allosteric protein, whereas myoglobin is not. This difference is expressed in three ways:

- 1. The binding of O_2 to hemoglobin enhances the binding of additional O_2 to the same hemoglobin molecule. In other words, O_2 binds cooperatively to hemoglobin. In contrast, the binding of O_2 to myoglobin is not cooperative.
- 2. The affinity of hemoglobin for oxygen depends on pH, whereas that of myoglobin is independent of pH. The CO_2 molecule also affects the oxygen-binding characteristics of hemoglobin.
- 3. The oxygen affinity of hemoglobin is further regulated by organic phosphates such as 2,3-bisphosphoglycerate (BPG). The result is that hemoglobin has a lower affinity for oxygen than does myoglobin.

OXYGEN BINDS COOPERATIVELY TO HEMOGLOBIN

The saturation Y is defined as the fractional occupancy of the oxygen-binding sites. The value of Y can range from 0 (all sites empty) to 1 (all sites filled). A plot of Y versus pO_2 , the partial pressure of oxygen, is called an oxygen dissociation curve. The oxygen dissociation curves of myoglobin and hemoglobin differ in two ways (Figures 7-21 and 7-22). For any given pO_2 , Y is higher for myoglobin than for hemoglobin. This means that myoglobin has a higher affinity for oxygen than does hemoglobin. Oxygen affinity can be characterized by a quantity called P_{50} , which is the partial pressure of oxygen at which 50% of sites are filled (i.e., at which Y = 0.5). For myoglobin, P_{50} is typically 1 torr, whereas for hemoglobin, P_{50} is 26 torrs.

The second difference is that the oxygen dissociation curve of myoglobin is hyperbolic, whereas that of hemoglobin is sigmoidal. Let us consider these curves in quantitative terms, starting with the one for myoglobin be-

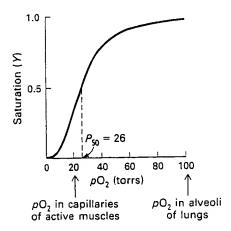


Figure 7-22 Oxygen dissociation curve of hemoglobin. Typical values for pO_2 in the capillaries of active muscle and in the alveoli of the lung are marked on the horizontal axis. Note that P_{50} for hemoglobin under physiological conditions lies between these values.